WEST Search History

DATE: Monday, August 18, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR		
L4	L2 and (agitation or agitating) adj5 (independent or independence)	0	L4
L3	L2 and agitation adj5 (independent or independence)	0	L3
L2	L1 and (multiple adj3 unit or multi-unit)	114	L2
L1	(hydroxypropyl adj3 cellulose or hydroxypropylcellulose or hpc) and (drug or medicament) same (particle or pellet or granule) and capsule and tablet	2091	L1

END OF SEARCH HISTORY

L2: Entry 6 of 12 File: USPT Jul 13, 1999

DOCUMENT-IDENTIFIER: US 5922352 A
TITLE: Once daily calcium channel blocker tablet having a delayed release core

Detailed Description Text (28):
A 102 g portion of the hydroxypropyl cellulose (Klucel EF) is dissolved in 2 kg of water and the nifedipine is dispersed into the solution to form a granulating suspension. A mixture of 612 g of hydroxypropyl cellulose (Klucel HXF), 2143 g of hydroxypropyl cellulose (Klucel EF) and 735 g of anhydrous lactose were granulated in a fluidized bed. The dried granulation is sized and mixed with 82 g of glyceryl monostearate.

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Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR		
L5	L4 and capsule and tablet and (sustained or controlled) adj3 release	15	L5
L4	(hydroxypropylcellulose or hpc or hydroxypropyl adj3 cellulose) and (active adj3 ingredient or drug or medicament) same (suspension or matrix) and (multi adj3 unit or multi-unit)	21	L4
L3	L2 and capsule	3	L3
L2	(hydroxypropylcellulose or hpc or hydroxypropyl adj3 cellulose) same nifedipine same (matrix or suspension)	12	L2
L1	hydroxypropylcellulose same nifedipine same (matrix or suspension)	4	L1

END OF SEARCH HISTORY

L5: Entry 12 of 15 File: USPT Aug 17, 1993

DOCUMENT-IDENTIFIER: US 5236689 A
TITLE: Multi-unit delivery system

Brief Summary Text (3):
This invention relates to patterned drug delivery. More particularly, this invention relates to patterned drug delivery by means of a plurality of individual drug delivery units or tablets. Still more particularly, but without limitation thereto, this invention relates to delivery of agents orally or in other media in a preprogrammed delivery profile.

Brief Summary Text (7):
The terms "drug unit," "dosage unit," "active agent unit" and "active agent dosage unit" as used herein include units that are capable of maintaining their physical configuration and chemical integrity while housed within the dispenser. This includes, without limitation, tablets with or without a density element; matrix tablets; pellets and elongated tablets where the height-to-diameter ratio exceeds one; capsules; elementary osmotic pumps, such as that described in U.S. Pat. No. 3,845,770; mini-osmotic pumps, such as those described in U.S. Pat. Nos. 3,995,631, 4,034,756 and 4,111,202; and multichamber osmotic systems referred to as push-pull and push-melt osmotic pumps, such as those described in U.S. Pat. Nos. 4,320,759 and 4,449,983; all of which are incorporated herein by reference.

Brief Summary Text (10):
The concept of patterned drug delivery covers a broad range of systems from time-release capsules whose components have coatings which erode at different rates, to controlled release rate tablets which operate by osmosis.

Brief Summary Text (11):
Despite the development of the art, however, there remains a continuing need for improved methods and systems for providing controlled drug release profiles.

Drawing Description Text (12):
FIG. 10 is a partial cross-sectional view of another embodiment of the housing for the dispenser for this invention with means for releasably holding an insert member comprising an expandable member for pushing tablets out of the dispenser.

Drawing Description Text (14):
FIG. 12 is a partial cross-sectional view of another embodiment of the housing for the dispenser of this invention having a tablet-containing section and a driving force section joined as releasable engaging structural member sections.

Detailed Description Text (9):
The drug units are in the form of a solid core or a matrix tablet or in any of a variety of forms which are capable of maintaining their physical and chemical integrity, i.e. do not substantially erode while in the housing. The driving member 34 operates to displace the units towards the exit port 22. As unit 24 comes into contact with the exit, it is dispensed into the environment and begins to deliver drug in a controlled or semi-controlled fashion. Once unit 24 is dispensed, linear displacement pushes unit 30 through the housing 20 so that it then comes into contact with exit 22 and is likewise dispensed. This continues until the dispenser is depleted of drug units.

Detailed Description Text (68):
Next, 15 kg of sodium chloride is milled in a mill to a number 21 size mesh screen. Then, 31.32 kg of the polymer granules of sodium Carbomer.RTM. is mixed with 13.68 kg of the milled sodium chloride, and the mix is blended for about an hour. Then, 455 g of magnesium stearate is added and the ingredients are blended for 10 minutes to produce a homogeneous expandable driving composition. The composition next is pressed into osmotically active tablets in a tablet press at a pressure of 500 lbs to produce a round, flat-faced 30 mg tablet.

Detailed Description Text (69):
The driving component is comprised of a semipermeable wall that surrounds a compartment for containing the osmotically active tablet. This wall is prepared as follows. First, 3.85 kg of cellulose acetate butyrate and 1.15 kg of tributyl citrate are dry mixed in a mixer for 5 minutes. This produces a polymer plasticizer blend of a 77/23 ratio for the semipermeable wall. Next, a rubber mill is used to melt-blend the blend, at a roller temperature of 70.degree. C. The blend is transferred to the moving rollers of the mill and mixed for 3 minutes. Then, after all the materials are added to the mill, the temperature is raised to 90.degree. C., followed by milling for 2 minutes. Next, the temperature is raised to 115.degree. C. and followed by two more minutes of milling, after which the temperature is increased to 133.degree. C. and followed by six minutes of milling the blend, after which the temperature is increased to 144.degree. C. and followed by six minutes of milling the blend. After the rollers are cooled to 50.degree. C., the blend is removed from the mill. The milled blend is cut into strips and passed through a grinder mill, and the resulting particles are fed into an injection molder and molded into the semipermeable wall surrounding a compartment with an opened end for receiving an expandable driving member and for mating with the dispensing component of the delivery system.

Detailed Description Text (71):
Next, the delivery system is assembled by first charging the subassembly (driving component) semipermeable walled member with three osmotic tablets. Then, microcrystalline wax is melted and the molten wax is poured on the top of the osmotic tablets to completely fill to the opened walled member. The charged subassembly is allowed to cool to room temperature.

Detailed Description Text (72):
Next, the delivery system subassembly (dispensing component) comprising the substantially impermeable wall surrounding the compartment is filled with a plurality of drug units in the form of compressed tablets, having the following composition: 90 wt % porcine somatotropin, 2 wt % polyvinylpyrrolidone, 1 wt % magnesium stearate, 3 wt % hydrogenated vegetable oil and 4 wt % histidine HCl. A suitable dosage of porcine somatotropin is about 112 mg per system. Therefore, the size and number of units will be designed accordingly. Then, the two subassemblies at their opened ends are joined by partially inserting the member comprising the osmotic tablets and the wax into the member comprising the drug units (layers). Next, 4 drops of moisture-cured cyanoacrylic adhesive are dropped into the remaining exposed surface, and the two members are fully inserted and twisted to effect a completed delivery system.

Detailed Description Text (79):
A swellable driving member was prepared as follows. 68.75 Weight percent Polyox.RTM. 303 (polyethylene oxide polymer), 5 wt % Carbopol.RTM. 934P (acidic carboxy polymer), 20 wt % sodium chloride, 5 wt hydroxypropylmethylcellulose and 1 wt % red ferric oxide (for coloring) were first passed through a 40-mesh screen and then mixed in a Hobart.RTM. blender. After the mixture was mixed for 15 minutes, ethanol was slowly added (0.1 mL/gm). The resulting wet granulation was passed through a 20-mesh screen before air drying overnight at room temperature. The dried granulation was passed through a 20-mesh screen and blended with magnesium stearate for 5 to 10 minutes. The composition was pressed into round, flat-faced, osmotically active tablets of 150 mg weight each.

Detailed Description Text (81):
An osmotically active tablet was placed in the end of one half of a size "0" hard gelatin capsule, after which three of the gemfibrozil drug units were added. A

fourth drug unit was placed in the end of the other half of the capsule, and the capsule halves were joined together at their open ends, by inserting one half into the other, and then sealed.

Detailed Description Text (82):
The sealed capsule was then covered with a rate-controlling membrane of the composition: 70 wt % cellulose acetate 398-10, 15 wt % polyethylene glycol 3350 and 15 wt % Klucel.RTM. EF (hydroxypropylcellulose). The membrane was scraped away at the end containing the drug units, exposing a portion of the gelatin capsule, to give an exit port of approximately 156 mil diameter. The resulting gemfibrozil delivery system had a 65% drug loading.

Detailed Description Text (85):
A dispenser according to Example V was prepared. The osmotically active tablet for the driving member had a weight of 250 mg and was composed of 68.5 wt % Polyox.RTM. 303, 10 wt % Carbopol.RTM. 934P, 15 wt % sodium chloride, 5 wt % hydroxypropylmethylcellulose, 1 wt % red ferric oxide and 0.5 wt % magnesium stearate.

Detailed Description Text (87):
One osmotically active tablet and five drug units were placed in a size "00" hard gelatin capsule. The capsule was joined and sealed and coated with the rate-controlling membrane according to Example V, and an exit port was made with an orifice diameter of approximately 250 mil.

Detailed Description Text (90):
A dispenser according to Example V was prepared, except that two gemfibrozil drug units were alternated with two non-drug-containing units (blanks) in the capsule so that the initial unit to be released from the exit port was a blank, followed by a drug unit, a blank, and, lastly, a drug unit. This provided a two-pulse delivery system. The in vitro release rate of the system (with the exit port pointing up) is shown in FIG. 16.

Detailed Description Text (98):
A swellable driving member was prepared as follows. Kappa-carrageenan (68.0 wt), polyvinylpyrrolidone (15.0 wt; K 29-32), sorbitol (14.0 wt %), potassium chloride (1.0 wt %) and red ferric oxide (1.0 wt %) were first passed through a 40-mesh screen and then mixed in a Hobart mixer for 5 min at low speed. Anhydrous denatured ethanol was added slowly with the mixer operating on low speed until a wet mass was formed. The resulting wet mass was passed through a 16-mesh screen and then air dried for 24 hr. The dried granulation was passed through a 16-mesh screen and blended with magnesium stearate (1.0 wt %; 80-mesh) in a roll mill for 5 min. The composition was pressed into round osmotically active tablets of 170 mg weight each, the tablets having one flat face and one convex face.

Detailed Description Text (99):
To assemble a delivery system, an osmotically active tablet was placed in the end of one half of a size "0" hard gelatin capsule. One of the flutamide drug units was placed into the capsule above the osmotic tablet, followed by one non-drug unit and then a second flutamide unit. The capsule halves were joined together at their open ends and firmly closed.

Detailed Description Text (100):
The closed capsule was then coated with 55 mg of a semipermeable membrane having the composition: 60.0 wt % cellulose acetate and 40.0 wt % hydroxypropylcellulose (Klucel.RTM. EF). The membrane was applied from an 80:20 (w:w) acetone:methanol solvent mixture with a 4% solids content. Systems were coated in a Wurster.RTM. coater with a 6-in diameter column. A 0.275 inch drug release orifice was then cut in the drug-containing end of each system through the membrane and the gelatin. After solvent coating, the systems were air dried for 24 hr before testing.

Detailed Description Text (108):
A first driving member was prepared following the procedures of Example IX but having the following composition: 58.5 wt % sodium carboxymethylcellulose, 35.0 wt % sodium chloride, 6.0 wt % HPMC, 0.25 wt % red ferric oxide and 0.25 wt % magnesium

stearate. The composition was pressed into round osmotically active tablets of 220 mg weight each and having one flat face and one convex face.

Detailed Description Text (109):
A second driving member was prepared having the same composition as the driving member in Example IX. The composition was pressed into round osmotically active tablets of 30 mg weight each and having two flat faces.

Detailed Description Text (110):
To assemble the device, a first osmotic driving member tablet was placed into a size "0" extended gelatin capsule, followed by a second osmotic driving member tablet, a flutamide tablet, a nondrug-containing tablet and, finally, a second flutamide tablet. Assembly was continued following the procedures of Example IX.